

Int'l Appl. No. : PCT/GB98/01627

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On page 58, line 2, after the sequence "gcgc AAG CTT gaa atc aaa egg GCC TCC ACA CAG AGC CCA" please insert --(SEQ ID NO:19)--.

On page 58, line 6, after the sequence "gcgc ctcgag TCA TTT ACC GGG ATT TAC AGA" please insert --(SEQ ID NO:20)--.

On page 59, line 7, after the sequence "GG ACT AGT AAT AGT GAC TCT GAA TGT CCC" please insert --(SEQ ID NO:21)--.

On page 59, line 11, after the sequence "ATT AGC GGC CGC TTA GCG CAG TTC CCA CCA CTT C" please insert --(SEQ ID NO:22)--.

On page 66, line 1, please cancel the word "CLAIMS" and substitute in its place --WHAT IS CLAIMED IS:--.

IN THE CLAIMS:

Cancel Claims 22, 23, 26, 30, 35, 39, and 44.

Amend the remaining claims as follows:

1. (Amended) A vector comprising a polynucleotide [sequence ("NS")] encoding [for] a [tumour]tumor-interacting protein [("TIP")] and optionally comprising a nucleotide sequence of interest ("NOI") which NOI encodes a product of interest ("POI"); wherein the [TIP]tumor-interacting protein is capable of recognizing a [tumour]tumor, [such that in use] and wherein the vector is capable of delivering [the NOI] a second polynucleotide of interest [and/or the POI] to the [tumour]tumor.

2. (Amended) [A]The vector according to claim 1 wherein the vector comprises the [NOI] second polynucleotide of interest.

3. (Amended) [A]The vector according to claim 2 wherein the [NOI] second polynucleotide of interest is [a] therapeutic [NOI and/or the POI is a therapeutic [POI] product of interest].

4. (Amended) [A]The vector according to [any one of the preceding claims]Claim 1 wherein [in use] the vector is capable of delivering the [NOI] second polynucleotide of interest [and/or the POI] to the interior of a [tumour]tumor mass.

5. (Amended) [A]The vector according to [any one of the preceding claims]Claim 1 wherein the [TIP]tumor-interacting protein [is or] comprises a [tumour]tumor-binding protein [("TBP")].

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6. [A]The vector according to [any one of the preceding claims wherein the TIP is a TBP]Claim 1 wherein the second polynucleotide of interest expresses a protein product of interest.
7. (Amended) [A]The vector according to [any one of the preceding claims]Claim 1 wherein the [NS]polynucleotide [and/or the TIP] comprises at least one [tumour]tumor binding domain capable of interacting with at least one [tumour]tumor-associated cell surface molecule [("TACSM")].
8. (Amended) [A]The vector according to claim 7 wherein the [TACSM] tumor-associated cell surface molecule is selectively expressed on one cell type or on a restrictive number of cell types.
9. (Amended) [A]The vector according to [any one of the preceding claims]Claim 1 wherein [in use] the vector is capable of delivering the [NOI] second polynucleotide of interest [and/or the POI] to a selective [tumour]tumor site.
10. (Amended) [A]The vector according to [any one of the preceding claims]Claim 1 wherein the [TIP]tumor-interacting protein [is or] comprises at least part of an antibody.
11. (Amended) [A]The vector according to [any one of the preceding claims]Claim 1 wherein the [TIP]tumor-interacting protein [recognises]binds to a tropoblast cell surface antigen.
12. (Amended) [A]The vector according to claim 11 wherein the [TIP recognises]tropoblast cell surface antigen is the 5T4 antigen.
13. (Amended) [A]The vector according to [any one of the preceding claims]Claim 1 wherein the [NS]polynucleotide [and NOI and/or the TIP] and [POI] second polynucleotide of interest are [linked together]expressed as a fusion protein.
14. (Amended) [A]The vector according to claim [13]6 wherein the [TIP]tumor-interacting protein and [POI] product of interest are [directly linked together]expressed as a fusion protein.
15. (Amended) [A]The vector according to [any one of the preceding claims]Claim 1 wherein [any one or more of] any nucleotide sequence selected from the group consisting of : the [NS, NOI, TIP] polynucleotide encoding the tumor-interacting protein, the

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second nucleotide sequence of interest, and both [and the POI] further comprises a polynucleotide sequence which encodes at least one additional functional component.

16. (Amended) [A]The vector according to [any one of the preceding claims]Claim 6 wherein any protein selected from the group consisting of: [at least] the [TIP]tumor-interacting protein, [and/or POI] the product of interest, and both, further comprises at least one additional functional component.

17. (Amended) [A]The vector according to claim 15 [or 16] wherein the additional functional component is selected from [any one or more]the group consisting of a [signalling]signaling entity [(such as a signal peptide)], an immune enhancer, a toxin, [or]and a biologically active enzyme[, or a sequence coding for any of same].

18. (Amended) [A]The vector according to [any one of the preceding claims]Claim 1 wherein the [retroviral] vector comprises a [tumour specific promoter enhancer]retroviral vector.

19. (Amended) [A]The vector according to [any one of the preceding claims wherein the vector is a]Claim 18 wherein the retroviral vector comprises a tumour specific promoter enhancer.

20. (Amended) A method of delivering a polynucleotide [sequence] of interest [("NOI") and/]or a product of interest [("POI") encoded by same]said polynucleotide of interest to a [tumour, wherein]tumor, comprising:

delivering the [NOI] polynucleotide of interest [and/]or [POI] product of interest [are delivered] to [the tumour]said tumor by use of [a]the vector of claim 1[comprising the NOI and/or expressing the POI; wherein the NOI and/or the POI is capable of recognizing a tumour; wherein the NOI and/or the POI is delivered to the tumour; and wherein the vector is a vector according to any one of the preceding claims].

21. (Amended) [A]The method according to claim 20 wherein the vector is used to deliver the [NOI] polynucleotide of interest and/[or POI] product of interest *ex vivo* [and/or *in vivo*] to the [tumour]tumor.

24. (Amended) A method of treating [a subject in need of same]cancer in a mammal, the method comprising delivering a polynucleotide [sequence] of interest [("NOI")] [and/]or a product of interest [("POI") encoded by same] to a [tumour]tumor, wherein the [NOI] polynucleotide of interest [and/]or [POI] product of interest are delivered to the

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[tumour]tumor by use of [a vector comprising the NOI and/or expressing the POI; wherein the NOI and/or the POI is capable of recognising a tumour; wherein the NOI and/or the POI is delivered to the tumour; and wherein the vector is a] the vector according to [any one of the preceding claims]claim 1.

25. (Amended) [A]The method according to claim 24 wherein the vector is used to deliver the [NOI] nucleotide sequence of interest [and/]or [POI] product of interest *ex vivo* [and/or *in vivo*]to the [tumour]tumor.

27. (Amended) A gene delivery system for targeting one or more genes encoding a [TIP]tumor-interacting protein [(preferably a TBP)] to a [tumour]tumor, comprising a genetic vector encoding a [TIP]tumor-interacting protein [(preferably a TBP)] and an *in vivo* gene-delivery system.

28. (Amended) A method of treating cancer comprising administering [at least one TIP (preferably at least one TBP) gene to a]the gene delivery system according to claim 27 [either systemically or directly] to the site of a [tumour]tumor.

29. (Amended) [A]The method [gene delivery system for introducing one or more genes encoding a TIP (preferably a TBP) into cells] of claim 28 wherein the tumor is of the haematopoietic [(preferably myeloid haematopoietic)] cell lineage [either *in vivo* or *ex vivo*].

31. (Amended) A genetic vector comprising a [therapeutic gene or genes]polynucleotide encoding a [TIP]tumor-interacting protein [(preferably a TBP),] operably linked to an expression regulatory element selectively functional in a cell type present within a [tumour]tumor mass.

32. (Amended) [A]The genetic vector of claim 31 additionally comprising [a therapeutic gene or genes is delivered to the interior of the tumour wherein the therapeutic gene encodes a TIP (preferably a TBP), which additionally contains] one or more effector domains.

33. (Amended) A method of treating cancer in a mammal which comprises administering [to an individual] a combination of a cytokine or a cytokine-encoding gene and one or more [TIP]tumor-interacting protein [(preferably a TBP)] genes.

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34. (Amended) [The delivery of] A method of delivering a gene to the site of a tumor comprising: [TIP]delivering tumor-interacting protein [- (preferably a TBP-)] encoding genes to the site of a [tumour]tumor.

36. (Amended) [A]The vector of Claim 14 wherein the [comprising (a) a NS coding for a TIP and (b) an NOI which encodes a POI; wherein the TIP is capable of recognising a tumour such that in use the vector is capable of delivering the NOI and/or the POI to the tumour; wherein the TIP and POI are fused to each other; and wherein the POI]fusion protein is capable of being secreted.

37. (Amended) [Use of] A method for producing a nucleotide sequence of interest comprising constructing the vector of Claim 1 and growing said vector in a compatible cell [a vector according to any one of the preceding claims as an *in situ* production factory of any one or more of the NS, NOI, POI and TIP].

38. (Amended) [Use of a vector according to any one of the preceding claims when] A method for delivering a polynucleotide sequence to a second cell comprising placing a first cell containing the vector of claim 1 in close association with the second cell [present in a cell to deliver any one or more of the NS, NOI, POI and TIP to a neighbouring cell].

40. (Amended) A process for preparing a [TBP]tumor-binding protein comprising expressing a [NS]polynucleotide encoding a [TBP]tumor-binding protein in a vector according to claim 1 **[4 or any claim dependent thereon].**

41. (Amended) A [TBP]tumor-binding protein wherein the [TBP]tumor-binding protein is selected from a group consisting of: 5T4ScFv.1, 5T4Sab1, 5T4ScFv-IgG, 5T4ScFv-IgE1, B7-1.5T4.1, B7-1.5T4.2 and B7-EGF.

42. (Amended) A [TBP]tumor-binding protein obtained by the process of claim 40 **[or the TBP of claim 41 for subsequent use in a medical application].**

43. (Amended) A method for diagnosis of cancer comprising: identifying or quantitating the tumor using the[TBP]tumor-binding protein according to claim 42 **[wherein the medical application is a diagnostic application].**

45. (Amended) [Use] A method for the prognosis of cancer comprising: identifying and/or quantitating [of] a [TACSM]tumor-associated cell surface molecule [as defined in claim 7 or claim 8 as a prognostic factor and/or a target for cancer therapy].

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46. (Amended) [Use of a TACSM according to]The method of claim 45 wherein the [TACSM]tumor-associated cell surface molecule is erb-2.

Please add the following claims:

47. The vector according to Claim 1 wherein the vector is capable of delivering the protein product of interest to the interior of a tumor mass.
48. The vector of Claim 17 wherein the signaling entity is a signal peptide.
49. The method according to claim 20 wherein the vector is used to deliver the polynucleotide of interest and/or product of interest *in vivo* to the tumor.
50. The method according to claim 24 wherein the vector is used to deliver the nucleotide sequence of interest and/or product of interest *in vivo* to the tumor.
51. The gene delivery system of Claim 27 wherein the tumor-interacting protein is a TBP.
52. The method of Claim 28 wherein the gene delivery system is administered systemically.
53. The method of Claim 28 wherein the gene delivery system is administered directly to the site of the tumor.
54. The method of Claim 30 wherein the haematopoietic lineage is a myeloid lineage.
55. The method of Claim 30 wherein the gene delivery system is administered *in vivo*.
56. The method of Claim 30 wherein the gene delivery system is administered *ex vivo*.
57. The genetic vector of Claim 31 wherein the tumor-interacting protein is a tumor binding protein.
58. The method of Claim 33 wherein the tumor-interacting protein is a tumor binding protein.
59. The method of Claim 33 wherein the tumor-interacting protein is a tumor binding protein.
60. The vector of Claim 40 wherein the protein product of interest is therapeutic.

IN THE SEQUENCE LISTING

Please cancel from the application Original Sequence Listing pages 63-65 and substitute therefore the attached Replacement Sequence Listing pages 1-9. Please consecutively renumber all pages following the canceled Original Sequence Listing.